THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Shrotri M, Navaratnam AMD, Nguyen V. Spike-antibody waning after second dose of BNT162b2 or ChAdOx1. *Lancet* 2021; published online July 15. http://dx.doi.org/10.1016/S0140-6736(21)01642-1.

Spike-antibody levels over time since the second dose of BNT162b2 or ChAdOx1 (Virus Watch)

Madhumita Shrotri, Annalan M D Navaratnam, Vincent Nguyen, Thomas Byrne, Cyril Geismar, Ellen Fragaszy, Sarah Beale, Wing Lam Erica Fong, Parth Patel, Jana Kovar, Andrew C Hayward, Robert W Aldridge

on behalf of the Virus Watch Collaborative

Supplementary Materials

I. Virus Watch Collaborative contributing authors list

Robert W Aldridge	University College London, London, UK
Anna Aryee	University College London, London, UK
Sarah Beale	University College London, London, UK
Isobel Braithwaite	University College London, London, UK
Thomas Byrne	University College London, London, UK
Tao Cheng	University College London, London, UK
Andrew Copas	University College London, London, UK
Ingemar Cox	University College London, London, UK
Wing Lam Erica Fong	University College London, London, UK
Ellen Fragaszy	University College London, London, UK London School of Hygiene & Tropical Medicine, London, UK
Cyril Geismar	University College London, London, UK
Jo Gibbs	University College London, London, UK
Richard Gilson	University College London, London, UK
Pia Hardelid	University College London, London, UK
Andrew C Hayward	University College London, London, UK
Anne M Johnson	University College London, London, UK
Ben Killingley	University of Nottingham, Nottingham, UK University College London Hospital, London, UK
Jana Kovar	University College London, London, UK
Vasileios Lampos	University College London, London, UK
Yunzhe Liu	University College London, London, UK
Rachel A McKendry	University College London, London, UK
Susan Michie	University College London, London, UK
Faith Miller	University College London, London, UK
Eleni Nastouli	University College London Hospital, London, UK Francis Crick Institute, London, UK
Annalan M D Navaratnam	University College London, London, UK
Nicholas Patni	University College London, London, UK
Aimee Serisier	University College London, London, UK
Madhumita Shrotri	University College London, London, UK
Colette Smith	University College London, London, UK
Moira Spyer	Francis Crick Institute, London, UK
Alison Rodger	Royal Free London NHS Foundation Trust, London, UK University College London Hospital, London, UK
Sophie Weber	University College London, London, UK
Linda Wijlaars	University College London, London, UK

II. Contributors

Study Conceptualisation: All authors. Project administration: JK, VN, SB, TB, AMDN, MS. Data curation: VN, AMDN, MS. Formal analysis: MS, RWA. Writing (original draft preparation): MS, RWA, ACH. Writing (review and editing): All authors. All authors had full access to the data used in the study. ACH and RWA have shared responsibility for the decision to submit for publication.

III. Additional Methods – definitions of clinical vulnerability

Clinically extremely vulnerable

Individuals were categorised as extremely clinically vulnerable using criteria set out by Public Health England and the Department of Health and Social Care as part of the guidance for shielding (https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19), which were adapted in line with clinical variables collected through the Virus Watch baseline survey, as follows:

Clinically extremely vulnerable (CEV) criteria as per PHE/DHSC	**Inclusion in Virus Watch CEV definition**
Solid organ transplant recipients	Included
Cancer undergoing active chemotherapy	Included
Cancers undergoing radical radiotherapy	All radiotherapy included (radical radiotherapy was not ascertained)
Cancer of blood or bone marrow	Included
Immunotherapy or antibody treatments for cancer	Included
Targeted cancer therapies affecting the immune system	Included
Bone marrow or stem cell transplant in last 6 months or still taking immunosuppressive drugs	Included if still taking immunosuppressive drugs (those who received a transplant in the last 6 months but not on immunosuppression were not ascertained).
Severe respiratory conditions including all cystic fibrosis, severe asthma and severe chronic obstructive pulmonary disease (COPD)	All asthma, COPD and cystic fibrosis included (severity was not ascertained)
Rare diseases that significantly increase the risk of infections (such as severe combined immunodeficiency (SCID), homozygous sickle cell disease)	Sickle cell disease included (other immunodeficiencies were not ascertained)
Immunosuppressive therapies sufficient to significantly increase risk of infection	Not included unless meets any of the criteria above, but are included in 'clinically vulnerable' (specific immunosuppressive therapies were not ascertained)
Problems with spleen, including splenectomy	Included
Down's syndrome	Not included (as not distinguished from other learning disabilities)
Chronic kidney disease Stage 5 or on renal dialysis	All CKD was included (stage and dialysis requirement were not ascertained)
Pregnancy with significant heart disease	Not included (up to date information on pregnancy was not available)

Others classified as clinically extremely vulnerable	Not included

Clinically vulnerable

Individuals were categorised as clinically vulnerable (CV) using criteria set out by the Joint Committee on Vaccination and Immunisation (https://www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-30-december-2020), excluding those who met the superseding clinically extremely vulnerable (CEV) criteria. Clinical vulnerability criteria were adapted in line with clinical variables collected through the Virus Watch baseline survey, as follows:

Clinically vulnerable (CV) criteria as per JCVI	**Inclusion in Virus Watch CV definition**
chronic respiratory disease, including chronic obstructive pulmonary disease (COPD), cystic fibrosis and severe asthma	Not included (included in CEV)
chronic heart disease (and vascular disease)	Included
chronic kidney disease	Not included (included in CEV)
chronic liver disease	Included
chronic neurological disease including epilepsy	Included
Down's syndrome	Included as part of broader learning disabilities
Severe and profound learning disability	All learning disabilities included (severity was not ascertained)
Diabetes	Included
Solid organ, bone marrow and stem cell transplant recipients	Not included (included in CEV)
People with specific cancers	All cancers included, except those that met CEV criteria
Immunosuppression due to disease or treatment	Included, except those that met CEV criteria
Asplenia and splenic dysfunction	Not included (included in CEV)
Morbid obesity	Included
Severe mental illness	Not included (severity of mental illness was not ascertained)

IV. Supplementary Tables

Table S1. Characteristics of Included Participants

	N	% of total
Total	**605**	***100.0***
Male	284	*46.9*
Female	321	*53.1*
18-64 years	**348**	***57.5***
18-34	15	*2.5*
35-49	38	*6.3*
50-64	295	*48.8*
65+ years	**257**	***42.5***
65-79	254	*42.0*
80+	3	*0.5*
Not clinically vulnerable	302	*49.9*
Clinically vulnerable (CV)	186	*30.7*
Clinically extremely vulnerable (CEV)	117	*19.3*
Vaccine type, N-serostatus, and dose interval in days for N-seronegatives		
Pfizer (BNT162b2)	**197**	***32.6***
Void result for N	1	*0.2*
N-seropositive	19	*3.1*
N-seronegative	177	*29.3*
21-28 days	2	*0.3*
29-56 days	6	*1.0*
57-84 days	152	*25.1*
>84 days	6	*1.0*
Missing dose 1 date	11	*1.8*
Oxford/AZ (ChAdOx1)	**405**	***66.9***
Void result for N	0	*0.0*
N-seropositive	28	*4.6*
N-seronegative	377	*62.3*
21-28 days	0	*0.0*
29-56 days	17	*2.8*
57-84 days	349	*57.7*
>84 days	5	*0.8*
Missing dose 1 date	6	*1.0*
Vaccine type missing	**3**	***0.5***
Analysis of antibody levels over time since dose 2 in days *(N-seronegatives excl. dose interval 21-28 days)*		
Pfizer (BNT162b2)	**175**	***28.9***
0-20 days	0	*0.0*
21-41 days	53	*8.8*
42-55 days	58	*9.6*
56-69 days	44	*7.3*
70+ days	20	*3.3*
Oxford/AZ (ChAdOx1)	**377**	***62.3***
0-20 days	46	*7.6*
21-41 days	180	*29.8*
42-55 days	100	*16.5*
56-69 days	39	*6.4*
70+ days	12	*2.0*

Table S2. BNT162b2 - S-antibody levels over time and by demographic or clinical groupings

	Days since second dose	*N*	Median	25th Centile	75th Centile	p-value for trend
Pfizer - BNT162b2						
Overall	0-20d	*0*	-	-	-	
	21-41d	53	7,506	4,925	11,950	<0.001
	42-55d	58	6,359	3,633	9,965	
	56-69d	44	3,920	2,168	6,989	
	70+d	20	3,320	1,566	4,433	
Male	0-20d	*0*	-	-	-	
	21-41d	*26*	6,745	3,475	11,542	0.001
	42-55d	*28*	5,304	3,070	8,759	
	56-69d	*23*	3,596	1,989	7,383	
	70+d	*10*	2,604	527	4,482	
Female	0-20d	*0*	-	-	-	
	21-41d	*27*	8,203	5,890	12,702	<0.001
	42-55d	*30*	6,726	4,054	11,724	
	56-69d	*21*	4,028	2,347	6,235	
	70+d	*10*	3,553	2,685	4,316	
18-64 years	0-20d	*0*	-	-	-	
	21-41d	*35*	8,203	5,311	13,416	0.001
	42-55d	*23*	7,393	4,761	12,820	
	56-69d	*16*	4,200	2,595	7,074	
	70+d	*8*	3,809	2,909	5,344	
65+ years	0-20d	*0*	-	-	-	
	21-41d	*18*	6,288	3,123	9,548	<0.001
	42-55d	*35*	5,271	3,385	9,070	
	56-69d	*28*	3,704	2,168	6,989	
	70+d	*12*	2,604	695	4,350	
Not Clinically Vulnerable	0-20d	*0*	-	-	-	<0.001
	21-41d	*23*	10,383	5,311	13,416	
	42-55d	*25*	6,356	4,032	8,829	
	56-69d	*23*	5,195	2,416	7,967	
	70+d	*8*	2,909	1,704	4,101	
Clinically Vulnerable (CV)	0-20d	*0*	-	-	-	0.002
	21-41d	*23*	7,281	3,922	12,702	
	42-55d	*23*	6,362	3,250	9,295	
	56-69d	*10*	3,732	1,361	7,366	
	70+d	*8*	3,577	1,408	4,350	
Clinically Extremely Vulnerable (CEV)	0-20d	*0*	-	-	-	0.112
	21-41d	*7*	5,391	3,071	9,548	
	42-55d	*10*	6,889	3,633	14,036	
	56-69d	*11*	3,812	1,178	6,235	
	70+d	*4*	4,647	1,957	7,278	

Table S3. ChAdOx1 - S-antibody levels over time and by demographic or clinical groupings

	Days since second dose	*N*	Median	25th Centile	75th Centile	p-value for trend
Oxford/AZ – ChAdOx1						
Overall	0-20d	*46*	1,201	609	1,865	
	21-41d	*180*	964	533	1,545	<0.001
	42-55d	*100*	714	397	1,222	
	56-69d	*39*	757	382	984	
	70+d	*12*	190	67	644	
Male	0-20d	*19*	981	589	1,865	
	21-41d	*86*	856	498	1,326	0.007
	42-55d	*44*	827	459	1,611	
	56-69d	*22*	695	382	852	
	70+d	*3*	144	24	217	
Female	0-20d	*27*	1,233	609	2,132	
	21-41d	*94*	1,050	743	1,771	<0.001
	42-55d	*56*	612	373	1,051	
	56-69d	*17*	924	427	1,192	
	70+d	*9*	237	74	718	
18-64 years	0-20d	*46*	1,201	609	1,865	
	21-41d	*135*	1,028	624	1,552	<0.001
	42-55d	*34*	569	371	1,048	
	56-69d	*12*	695	525	1,031	
	70+d	*5*	217	74	718	
65+ years	0-20d	*0*	-	-	-	
	21-41d	*45*	830	460	1,386	0.032
	42-55d	*66*	763	480	1,337	
	56-69d	*27*	817	248	984	
	70+d	*7*	163	24	570	
Not Clinically Vulnerable	0-20d	*25*	1,168	621	2,132	
	21-41d	*102*	946	624	1,762	0.002
	42-55d	*46*	827	474	1,063	
	56-69d	*18*	647	382	968	
	70+d	*3*	718	163	1,002	
Clinically Vulnerable (CV)	0-20d	*12*	1,575	847	2,549	0.053
	21-41d	*48*	828	403	1,502	
	42-55d	*31*	723	443	1,337	
	56-69d	*14*	835	512	1,045	
	70+d	*3*	144	23	570	
Clinically Extremely Vulnerable (CEV)	0-20d	*9*	882	609	1,233	0.002
	21-41d	*30*	1,050	740	1,290	
	42-55d	*23*	466	152	1,826	
	56-69d	*7*	677	221	917	
	70+d	*6*	145	60	237	

V. Supplementary Figure

***Figure*: Spike-antibody levels with time since second dose of vaccination in N-seronegative individuals with extended dose intervals stratified by vaccine type (a) and further stratified within vaccine type by sex (b, e), age (c, f), and clinical vulnerability status (d, g)**

p-values derived from non-parametric tests for trend for each sub-group are given in brackets within the panel legends.